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ARTICLE

Construction of a novel INHIBIT logic gate through fine-tuned assembly of anthryl fluorophore *via* selective anion recognition and host-guest interaction

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A novel ligand (**AAP**) based on an anthryl fluorophore was rationally designed and synthesized. The presence of $H_2PO_4^-$ (Pi) could induce the effective assembly of the ligand which leads to a strong excimer emission, while β-cyclodextrin (β-CD) dis-assembled the Pi-ligand complex through a host-guest interaction with terminal adamantane groups. This dis-assembly causes a considerable decrement of emissive intensity as well as a clear blue-shift of emissive wavelength. By manipulating the assembly and dis-assembly of antharyl fluorophore with Pi and β-CD, a novel INHIBIT logic gate was constructed using Pi and β-CD as the chemical inputs and fluorescence emission as the output.

1. Introduction

Molecular logic gate, mimicking the real functions of semiconductor logic gate in modern computing, extends the information processing to the molecular level and thus has attracted much attention in the field of supramolecular chemistry.[1-7] Since the discovery of the first AND gate in solution by A.P. de Silva,[8] molecular logic gate has experienced rapid growth and various types of logic gates, such as NAND, OR, XNOR, XOR, NOR, NOT and INHIBIT, have been established.[9-15] Among them, the INHIBIT gate involves a combination of AND and NOT logic functions and deserves increasing attention due to its non-commutative, in which the output signal is inhibited by only one powerful input.[16-19] The operation of INHIBIT gate is usually derived from some switchable molecular systems, especially by changing the optical properties. Despite the striking number of INHIBIT gates developed in recent years, their design mechanisms are controlled by intramolecular charge transfer (ICT),[20-21] photo-induced electron transfer (PET)[22] and fluorescent resonance energy transfer (FRET).[23] In this sense, development of INHIBIT logic gate with new design mechanisms is an attractive challenge.

Anthryl fluorophore was used to obtain novel multi-responsive fluorescent assembly and dis-assembly phenomena.[24-26] If one can tune the assembly properties of anthryl moiety by introducing different inputs, novel logic gates could be constructed. Until now, however, few relative reports were found with respect to logic gates built on the assembly of anthryl fluorophore to the best of our knowledge.

Anion-induced self-assembly has attracted much attention recently, since it provides a new and efficient strategy to build functional supramolecular structures. Beer and co-workers reported a novel anion-templating strategy for the construction of rotaxanes and catenanes as efficient anions sensors.[27-29] Wu and co-workers presented the anion-induced assembly process to build novel double and triple helical supramolecular structures.[30-31] In our previous work, a series of selective chemosensors containing anthryl fluorophore towards $H_2PO_4^-$ anions in polar solvents, even in aqueous solution were achieved.[32-34] In that case, the high selectivity is derived from the subtle control of the assembly of anthryl moiety by ligand structure, anions and solvent polarity.

In this work, a new ligand **AAP** was designed and synthesized as a potential INHIBIT logic gate. It is composed of two amide-pyridinium moieties as binding sites and an anthryl fluorophore as the signaling part. Adamantane group was introduced at the two terminals for controlling the assembly behavior *via* potential host-guest interaction with β-CD. The detailed design rationale is exhibited in **Fig. 1** and it is based on the following hypotheses: (1) under the role of Pi, the ligand **AAP** could assemble to form Pi-**AAP** complex according to our previous reports. In this case, two anthracene groups are located closer, which would lead to a different emissive wavelength compared with the pure ligand, (2) terminal adamantane moieties are known to be easily incorporated into the cavity of β-CD by host-guest interactions. If the formation of Pi-**AAP** complex could be disturbed by this host-guest interaction between adamantane and β-CD, the assembly behavior of anthryl fluorophore might change accordingly

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Electronic Supplementary Information (ESI) available: details of experimental procedures, characterization of ligand **AAP**, including ^{1}H NMR, ^{13}C NMR and HR-MS. See DOI: 10.1039/x0xx00000x

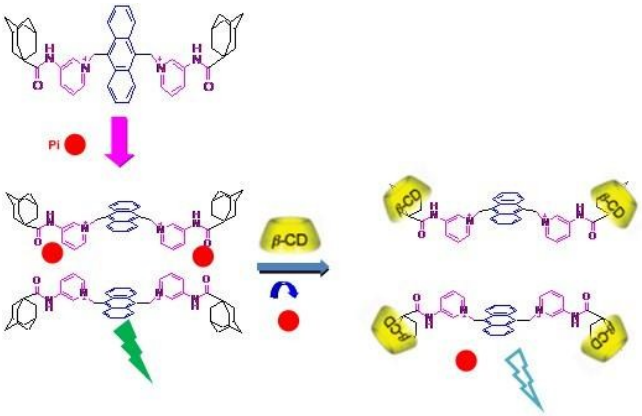


Fig. 1 Schematic representation of the proposed Pi-induced assembly and β-CD induced dis-assembly processes.

giving rise to differences in fluorescence property. In a word, taking advantage of Pi anion and β-CD as two different chemical inputs and fluorescence emission as the output, a potential INHIBIT logic gate will be achieved.

2. Experimental

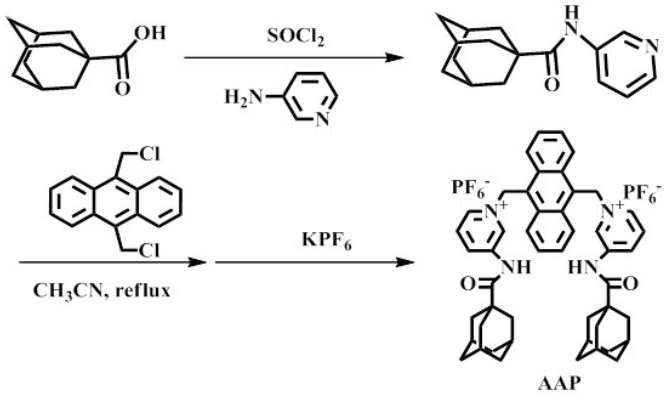
2.1 Material and Characterization

All the chemicals were purchased from commercial sources and used without further purification unless mentioned. Acetonitrile was pre-dried by shaking with type 4A molecular sieves, and then distilled over calcium hydride before use. Other solvents were used as received. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Av400 NMR spectrometer at 400 MHz and 126 MHz, respectively. Chemical shifts are given in parts per million (ppm) relative to tetramethylsilane (TMS). High resolution mass spectra (HRMS) were recorded on a Waters GC-TOF and LC/Q-TOF mass spectrometer. Fluorescence spectra were obtained from a Jasco FP-8300 spectrofluorometer. UV-vis absorption spectra were all taken on a Hitachi UV-4100 spectrophotometer. Quartz cells with 1 cm path length were used.

2.2 Synthetic procedures

The synthetic route of **AAP** was shown in **Scheme 1**.

Synthesis of N-(1-adamantoyl)-3-aminopyridine. N (1-adamantoyl)-3-aminopyridine was synthesized according to a reported method with some modifications.[35] 1-adamantanecarboxylic acid was converted into the acid chloride by treating with thionyl chloride at 80 °C in benzene for 3 hours, thus obtaining 1-adamantanecarbonyl chloride. After that, 3-aminopyridine (0.47 g, 5 mmol) and triethylamine (1.3 mL, 10 mmol) were suspended in 50 mL of dry benzene and cooled in an ice bath. To this suspension, a solution of 1-adamantanecarbonyl chloride (1.192 g, 6mmol) in dry benzene (50mL) was added dropwise under vigorous stirring. The mixture was stirred at 0℃ for another two hours and then allowed to obtain room temperature overnight. The solution



Scheme 1 Synthetic route of **AAP**.

was washed with water and the organic phase was dried over anhydrous $MgSO_4$. After filtration, the solvent was removed on a rotatory evaporator and purified by column chromatography with ethyl acetate as the eluent which gave N-(1-adamantoyl)-3-aminopyridine (0.97g, 76%) as a yellowish powder. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.35 (s, 1H), 8.83 (d, J = 1.9 Hz, 1H), 8.29 – 8.20 (m, 1H), 8.08 (d, J = 8.3 Hz, 1H), 7.32 (dd, J = 8.2, 4.7 Hz, 1H), 2.02 (s, 3H), 1.92 (s, 6H), 1.71 (s, 6H). The ^{1}H-NMR data are in agreement with those found in the literature.

Synthesis of AAP. To a 100 mL round bottom flask, N-(1-adamantoyl)-3-aminopyridine (0.769 g, 3 mmol) and 9,10-bis(chloromethyl)anthracene (0.413 g, 1.5 mmol) were added. Then dry CH_3CN (30 mL) was added and the suspension was heated to 82 ℃ and kept refluxing for 40 h until a yellow precipitate was formed. The precipitate was filtered and washed several times with CH_3CN. The crude product was purified by silica gel column chromatography (CH_2Cl_2:CH_3OH=5:3) to give a yellow solid. Then the yellow solid was dissolved in DMF. After dropwise addition of excess saturated aqueous KPF_6 solution, 50 mL H_2O was added in one portion and a light yellow precipitate was formed. The precipitate was filtered and washed with water repeatedly. After drying in vacuum, **AAP** (0.77 g, 58%) was obtained as a yellow powder which was used without further purification. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 10.15 (s, 2H), 9.68 (s, 2H), 8.61 (d, J = 8.6 Hz, 2H), 8.56 (dd, J = 6.9, 3.2 Hz, 4H), 8.37 (d, J = 6.1 Hz, 2H), 7.96 (dd, J = 8.6, 6.1 Hz, 2H), 7.77 (dd, J = 6.9, 3.1 Hz, 4H), 7.06 (s, 4H), 2.03 (s, 6H), 1.89 (s, 12H), 1.70 (d, J = 6.5 Hz, 12H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 177.18, 139.63, 137.86, 135.01, 134.80, 131.42, 130.56, 128.23, 128.15, 127.13, 126.01, 124.63, 56.21, 41.27, 37.85, 36.35, 35.75, 27.35, 26.82. ESI-MS calcd for $C_{48}H_{52}N_4O_2^{2+}$: 716.4090 $[M]^{2+}$; found: 358.2043(m/2z).

3. Results and Discussion

To verify our conjecture, the sensing ability of ligand **AAP** towards different anions was first studied to figure out the selectivity of anion-induced assembly properties of **AAP**. Pure **AAP** in CH_3CN exhibited almost no fluorescence owing to the quenching effect of photo-induced electron transfer (PET)

from anthryl moiety to pyridinium.[33] Among various anions tested, only Pi induced clear fluorescence change, while others such as I^-, F^-, OH^-, CN^-, Cl^-, Br^-, NO_3^- and AcO^-, showed neglectable changes (**Fig. 2a**), indicating that **AAP** can be used as the selective Pi sensing agent. This result is in accordance with our previous results. Compared with that of pure ligand, the Pi-**AAP** complex exhibited strong green fluorescence centered at 500nm, which is the well-known excimer emission of anthryl fluorophore,[32] confirming the anion-induced assembly of **AAP**.

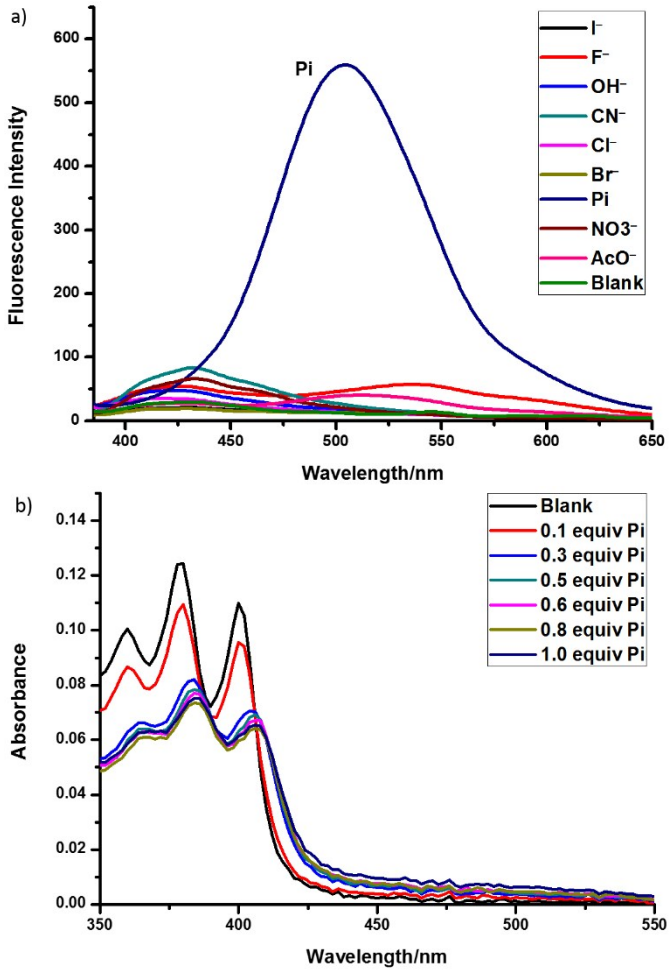


Fig. 2 (a) Fluorescence spectra of **AAP** (5.0 μM) upon addition of various anions (5 equiv) in CH_3CN (λ_{ex}=360 nm). (b) Absorption spectra of **AAP** (5.0 μM) upon addition of various amounts of Pi in CH_3CN.

UV-Vis absorption experiment provides further evidence about Pi-induced self-assembly of ligand **AAP**, by showing the apparent red-shift in absorption of anthryl fluorophore upon titration of Pi into ligand **AAP**. As reported, the longer wavelength absorption band compared with the pure **AAP** indicated the formation of association of anthryl fluorophore in ground state (**Fig. 2b**). The clear red-shift of the absorption bands of anthracene indicates the formation of J-aggregate.[36-38] The ^{1}H NMR spectra before and after the addition of Pi into **AAP** were also recorded and shown in **Fig. 3**. Protons of the anthryl moiety showed clear shifting towards higher magnetic field after the addition of 0.5 equiv Pi. This result further demonstrates the binding of Pi with **AAP**. **Fig. S5** shows the fluorescent titration data for **AAP** with Pi. The job plot for the binding between **AAP** and Pi showed a 1:1 stoichiometry (**Fig S6**). From the fluorescence titration, the binding constant and detection limit of **AAP** toward Pi was calculated to be $(5.3\pm0.1)\times10^5$ M^{-1} and 1.842×10^{-7} M respectively.

Once confirming the formation of Pi-**AAP** complex, which showed elegant assembled excimer emission of anthryl fluorophore, our attention transferred to how to dis-assemble or disturb this Pi-**AAP** complex aiming to change the fluorescence. Considering the selective binding between adamantane moiety and β-CD as previously reported, the fluorescence change due to the addition of β-CD into Pi-**AAP** complex was therefore investigated. Upon titration with β-CD, as shown in **Fig. 4a**, the excimer emission coming from Pi-**AAP** complex decreased. In contrast, a new fluorescence emission centered at about 440nm increased, which is the classical monomer emission of anthryl fluorophore. Accordingly, a clear fluorescence color change from green to blue was observed (**Fig. 4a inset**). This result indicated the dis-assembly behavior of Pi-**AAP** complex after the addition of β-CD. In UV-Vis absorption titration between Pi- **AAP** complex and β-CD, the apparent blue-shift of anthryl fluorophore further evidences the β-CD induced dis-association of Pi-**AAP** complex in ground state (**Fig. 4b**). The occurrence of dis-assembly Pi-**AAP** complex was due to the host -guest interaction between adamantane and β-CD. The ^{1}H NMR investigation of Pi-**AAP** complex solution before and after addition of β-CD evidences the formation host-guest complex. Signals of methylene protons on adamantyl group showed downfield shift after addition of β-CD (Fig. 3 inset).[39]

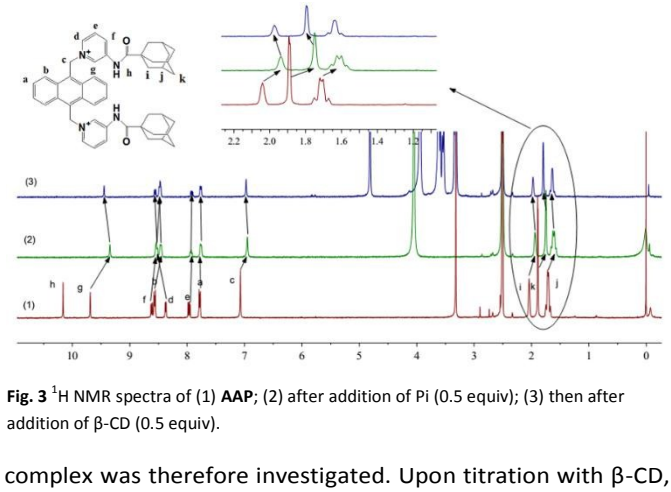
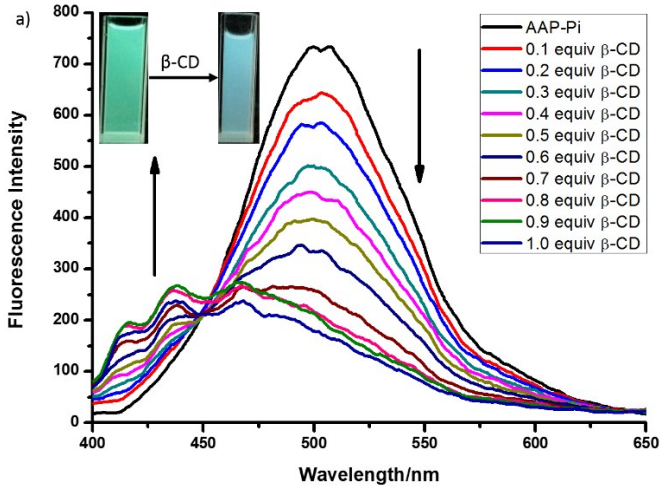


Fig. 3 ^{1}H NMR spectra of (1) **AAP**; (2) after addition of Pi (0.5 equiv); (3) then after addition of β-CD (0.5 equiv).



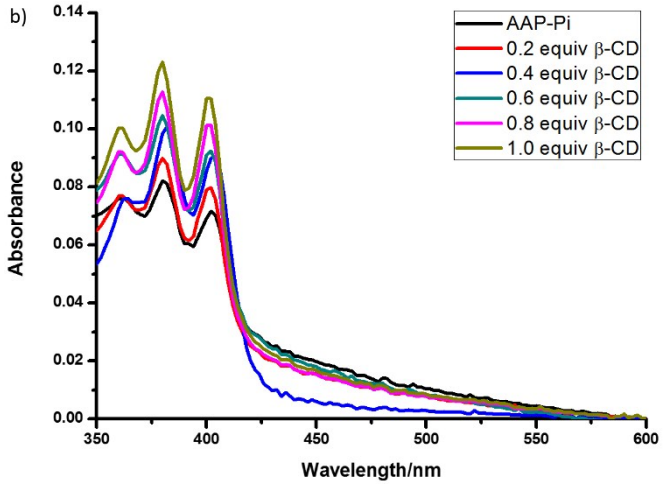


Fig. 4 (a) Fluorescence spectra of **AAP**-Pi complex (5.0 μM) upon addition of various amounts of β-CD in CH_3CN (λ_{ex}=360 nm). (b) Absorption spectra of **AAP**-Pi complex (5.0 μM) upon addition of various amounts of β-CD in CH_3CN.

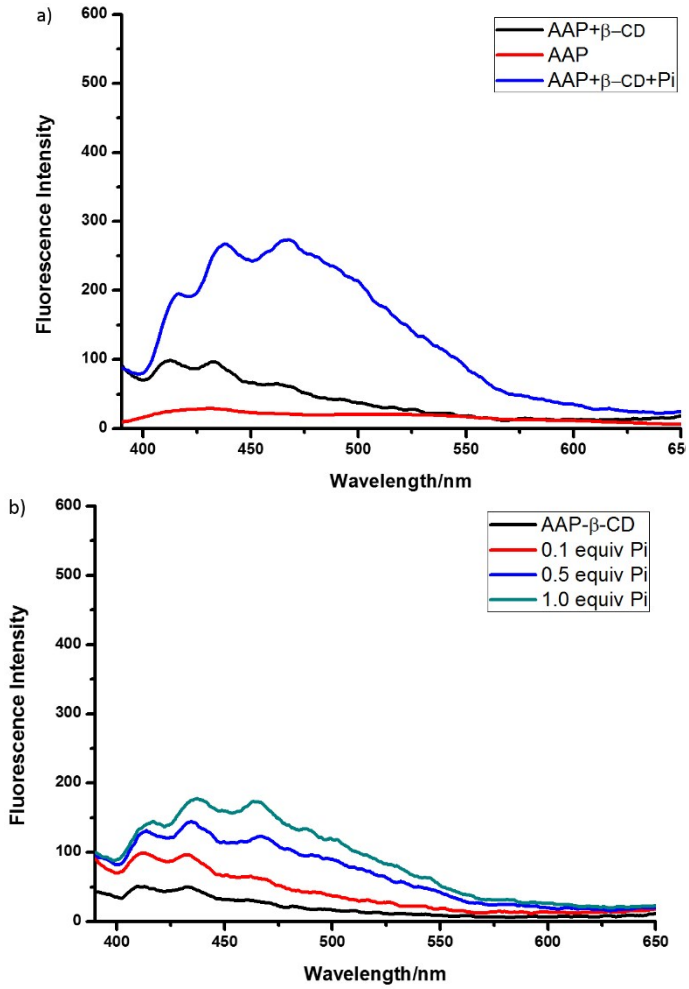


Fig. 5 (a) Fluorescence spectra of **AAP** (5.0 μM) upon addition of β-CD (1 equiv) and Pi (1 equiv) in CH_3CN (λ_{ex}=360 nm). (b) Fluorescence spectra of **AAP**-β-CD complex (5.0 μM) upon addition of different amounts of Pi in CH_3CN (λ_{ex}=360 nm)

Changes in fluorescence due to reverse addition of β-CD and Pi to **AAP** were also studied. Some interesting results obtained were shown in **Fig. 5**. When β-CD was first introduced into pure **AAP** solution instead of Pi, still rather weak fluorescence of anthryl fluorophore was obtained together with a subtle wavelength change. This result means the presence of host-guest interaction between adamantane and β-CD. More interestingly, when Pi was added into the **AAP**-β-CD complex solution, Pi-induced excimer emission was not found, enhancement of monomer emission was alone observed (**Fig. 5b**). This result indicated that the Pi-induced assembly of ligand **AAP** was inhibited by the formation of **AAP**-β-CD complex. As for the enhancement of monomer emission, it might be due to the block of photo-induced electron transfer (PET) from anthryl moiety to pyridinium by the interaction with Pi anions.

These results obtained above demonstrated clearly that the assembly phenomena of anthryl fluorophore in ligand **AAP** could be tuned by introducing Pi and β-CD as two chemical inputs. Pi could induce the assembly of **AAP** to give excimer emission, and β-CD could inhibit this Pi-induced assembly

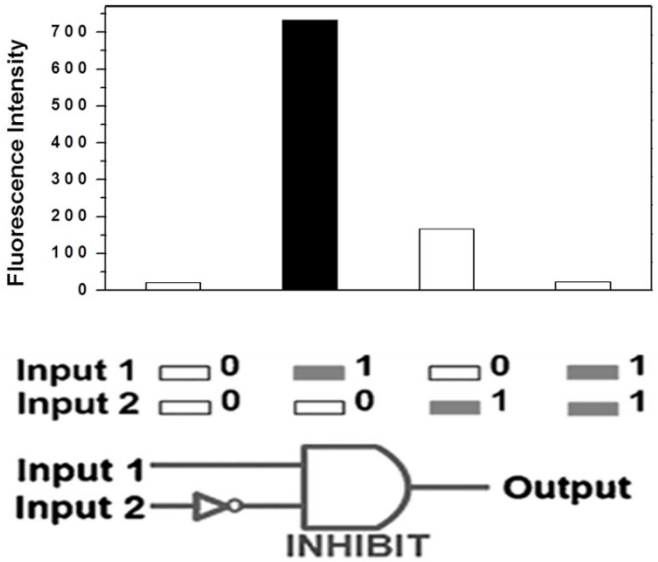


Fig. 6 Output and the corresponding truth tables for the INHIBIT gates (λ_{ex}=360 nm) of **AAP** using Pi (Input 1) and β-CD (Input 2) as inputs.

through the host-guest interaction. Accordingly, this system correlates very well with an INHIBIT logic gate as shown in **Fig. 6**. In considering the INHIBIT logic gate properties of **AAP**, in our system, Pi and β-CD act as two chemical inputs, while the excimer emission at 500 nm acts as the output. The output is "0" and the gate is "OFF" when (1) both the Pi and β-CD are absent, (2) β-CD alone is present, (3) both the Pi and β-CD are present. Correspondingly if the output is "1" and the gate is "ON" only when Pi alone is present. Thus, a new INHIBIT gate is constructed by controlling the assembly phenomena of anthryl fluorophore by inputting different chemical stimuli.

Conclusions

In summary, a potential INHIBIT logic gate based on an anthryl fluorophore was rationally designed and synthesized. Under the role of $H_2PO_4^-$, anthryl fluorophore could assemble to give apparent excimer fluorescent emission, while β-CD could inhibit this Pi-induced assembly process *via* host-guest interaction with adamantane moieties. Based on this phenomena, a novel INHIBIT gate was constructed. This is the

first example of INHIBIT gate that combines anion-induced assembly and host-guest triggered inhibition. Further work will be focused on the exploration of the detailed structure-property relationship for the construction of novel logic gates.

Acknowledgment

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Construction of a novel INHIBIT Logic gate through fine-tuned assembly of anthryl fluorophore via selective anion recognition and host-guest interaction

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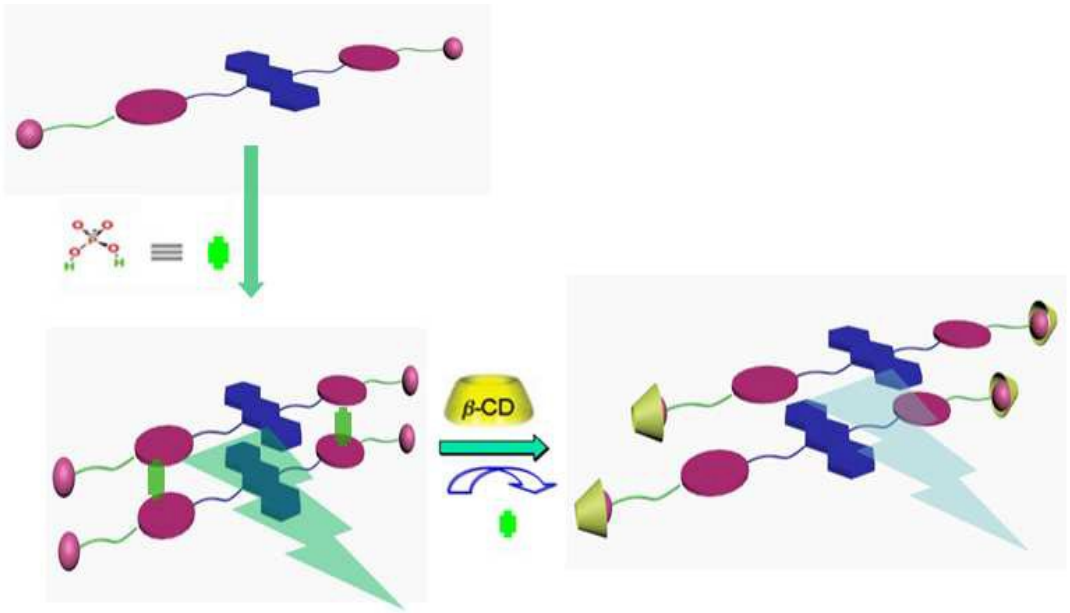

A novel Ligand **AAP** containing of anthryl fluorophore was achieved as per the rational design. $H_2PO_4^-$ (Pi) induced assembly of **AAP** leads to strong excimer emission, while β-CD dis-assembled the Pi-**AAP** complex through host-guest interaction. This dis-assembly causes a considerable decrement of emission. Thus assembly and disassembly of antharyl fluorophore by Pi and β-CD as chemical inputs and emission around 500 nm as output resulted in the construction of novel INHIBIT gate.